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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	7

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/132,799	Schoenrock et al.
Examiner	**Group Art Unit**
M. Borin	1631

X Responsive to communication(s) filed on *Dec 1, 1999*

X This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *1-12* is/are pending in the application.

Of the above, claim(s) *2, 5, and 7-10* is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) *1, 3, 4, 6, 11, and 12* is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

Status of the claims

1. Amendment filed 12/01/99 is acknowledged. Claims 1, 3-6 are amended. Claims 11,12 are added. Claims 1-12 are pending.

Applicants requested reconsideration of the restriction requirement. It is noted however, that applicant have elected Group I without traverse (see previous Office action, p. 4, paragraph 3). In regard to the election of species, it seems that applicant considers the election of species as final. This is not the case. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush - type claim and claims to the elected species shall be rejected, and claims to the non - elected species would be held withdrawn from further consideration. On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush - type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush - type claim with respect to a non - elected species, the Markush - type claim will be rejected and claims to the non - elected species held withdrawn from further consideration.

In regard to method claims, the restriction requirement clearly stated that if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. See previous Office action, p. 3, first full paragraph.

Claims 1, 3, 4, 6,11,12 are under examination. Claims 2,5, 7-10 remain withdrawn from consideration as being drawn to non-elected invention or non-elected species.

Sequence Listing

2. The sequence listing has been received and approved.

Claim Objections

3. Objection to claim 1 is withdrawn in view of amendments to the claim.

Claim Rejections - 35 U.S.C. § 112, second paragraph.

4. Rejection of claims 1, 3, 4, 6 under 35 U.S.C. 112, second paragraph is withdrawn in view of amendments to the claims.

Claim Rejections - 35 U.S.C. § 102 and 103.

5. Claims 1, 3 remain rejected under 35 U.S.C. 103(a) as obvious over Kohmura et al for the reasons of record (see Office action mailed 5/26/99, paragraph # 6).

Applicant argues that, although the reference shows inhibition of angiotensin-converting enzyme (ACE), it indicates that further research is required to make conclusion about physiological meaning of the described peptides in blood pressure regulation.

Examiner respectfully disagrees. While it may not be absolutely certain that the peptides described in Komura will be as effective in *in vivo* conditions as in *in vitro*, a *prima facie* case of obviousness does not require absolute predictability of success. See In re O'Farell, 7 USPQ2d 1673 (CAFC 1988). The reference teaches that AVVRP, PAVVRP, NPAVVRP, ANPAVVRP,

YANPAVVRP (i.e., peptides as instantly claimed, wherein ψ= 1-5, Ω=0), all exhibit a strong inhibitory effect on angiotensin-converting enzyme (ACE). It is notoriously well known in the art that ACE inhibitors reduce blood pressure. US Patents 4,595,431, 4,584,299, 4,568,675 are cited to illustrate the latter; the patents teach different ACE inhibitors, all of which are show to have blood pressure reducing activity. Applying the ACE inhibitors of Komura *in vivo* would have been expected to have pharmaceutical effect on blood pressure regulation. Thus, one skilled in the art would be motivated to prepare pharmaceutical compositions of said peptides and expect their pharmaceutical activity, in the absence of evidence to the contrary. No such evidence has been provided. The arguments of counsel can not take the place of evidence in the record.

In regard to the change of language from "pharmaceutical composition" to "dermatological topical composition", intended use of the composition are of little relevance in determining the patentability of the composition.

6. Claims 1, 3 remain rejected under 35 U.S.C. 103(a) as obvious over Kohmura et al. supra., and further in view of Atlas of Protein Sequence and Structure for the reasons of record (see Office action mailed 5/26/99, paragraph # 7). Applicant refers to the defects of the rejection over Komura. As discussed in the immediately preceding paragraph, the rejection over Komura is maintained.

7. Claims 1, 3, 4 remain rejected under 35 U.S.C. 103(a) as obvious over Kohmura et al. supra., and further in view of Bundgaard and Sumner-Smith for the reasons of record (see Office action

mailed 5 26 99, paragraph # 8). Applicant argues that neither of the secondary references cures the "defects" of the Komura reference. As discussed above (paragraph #5), the rejection over Komura is maintained. The secondary references have been used to illustrate the well established knowledge of use of pharmaceuticals in the form of prodrugs , such as acetyl or amido derivatives. As explained in the rejection, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to use peptides described by Kohmura in pharmaceutical compositions in a form of a prodrug analog having protected N- and/or C-termini with a reasonable expectation that such prodrugs will have at least similar effectiveness in inhibition of angiotensin-converting enzyme and regulation of related physiological processes.

8. Claims 1, 3 remain rejected under 35 U.S.C. 102(e) as anticipated by Steffens et al. (US Patent 5,681,721) for the reasons of record (see Office action mailed 5/26/99, paragraph # 9).

Applicant argues that Steffens reference describes pharmaceutical composition for internal use, whereas the claimed pharmaceutical composition is for topical use.

Steffens teaches that the referenced composition may comprise such well known in the art excipients as carrier materials, solvents, diluents, coloring and binding agents (col. 6, lines 4-9). In particular the compounds described in the reference are used as an aqueous solution (e.g., col. 11, line 50). A composition of a pharmaceutical in a carrier, such as aqueous solution, can be used either internally or externally (e.g., topically). Arguments related to the intended use of the composition are of little relevance in determining the patentability of the composition. *In re Pearson*, 494 F.2d 1399,

181 USPQ 641 (CCPA 1974). A mere statement of purpose or intended use in the preamble of a claim need not be considered in finding anticipation. The *prima facie* case becomes final if an applicant does not present adequate evidence or argument in rebuttal, in the absence of which the prior art compels the conclusion reached by Examiner. In re Spada, 15 USPQ2d 1655 (Fed. Cir. 1990).

9. Claims 1, 3 remain rejected under 35 U.S.C. 103(a) as obvious over Steffens et al., supra., and further in view of Atlas of Protein Sequence and Structure for the reasons of record (see Office action mailed 5/26/99, paragraph # 9).

Applicant points to alleged defects of Steffens reference. The rejection over Steffens is maintained (see previous paragraph); thus the instant rejection is also maintained.

10. Claims 1, 6 remain rejected, and newly submitted claims 11,12 are rejected under 35 U.S.C. 103(a) as obvious over Kohmura et al., supra, or Steffens et al., supra. As explained in the rejection, the difference between Applicant's claimed preparations and that of the prior art appears to be minor in nature, and the claimed preparations would have been *prima facie* obvious from the prior art disclosure because, in the absence of sufficient factual evidence or unexpected results to the contrary, the claims are directed to optimization of an "art recognized variable", i.e., optimization of concentration of active ingredient. Applicant failed to present any factual evidence or showing

of unexpected results. Instead, the applicant refers to the defects of the primary references. Note, however, that the rejections over primary references (paragraphs #5.8 above) is maintained.

In regard to the change of language from "pharmaceutical composition" to "dermatological topical composition", intended use of the composition are of little relevance in determining the patentability of the composition.

Prior art made of record

US Patents 4,595,431, 4,584,299, 4,568,675 are cited to illustrate that ACE inhibitors have blood pressure reducing activity.

Conclusion.

11. No claims are allowed

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Cecilia Tsang can be reached on (703) 308-0254. The fax telephone number for this group is (703) 305-3014. Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. The Art Unit of your application in the PTO has changed. To aid any papers for this application, all further correspondent should be directed to Art Unit 1631.

February 23, 2000

mlb